

Amendments to the Claims:

Please cancel claims 2, 6, 10, 14, 22, 25, 27-33, and 40-45, without prejudice. Please amend claims 7, 12, 16, 21, and 23 as follows. This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A method to produce an immunoglobulin with fully human variable region or an analog thereof, specific for a desired antigen, which method comprises:

administering said antigen or an immunogenic portion thereof to a nonhuman animal under conditions to stimulate an immune response, whereby said animal produces B cells that secrete immunoglobulin specific for said antigen; wherein said nonhuman animal is characterized by being substantially incapable of producing endogenous heavy or light immunoglobulin chain variable regions, but capable of producing human immunoglobulin variable regions; and recovering said immunoglobulin or analog.

2. Canceled.

3. (Original) The method of claim 1 wherein said recovering step comprises immortalizing B cells from said animal, screening the resulting immortalized cells for the secretion of said immunoglobulin, and

1) recovering immunoglobulin secreted by said immortalized B cells, or

2) recovering the genes encoding at least the variable region of said immunoglobulin from the immortalized B cells, and optionally modifying said genes; expressing said genes or modified forms thereof to produce immunoglobulin or analog; and recovering said immunoglobulin or analog.

4. (Original) The method of claim 1 wherein said recovering step comprises

recovering genes encoding at least the variable region of immunoglobulins from the primary B cells of the animal;

generating a library of said genes expressing the variable regions;

screening the library for a variable region with desired affinity for the antigen;

recovering the genes encoding said variable regions;

expressing said recovered genes to produce an immunoglobulin or analog containing said variable region and recovering said immunoglobulin or analog.

5. (Original) A recombinant DNA molecule comprising a nucleotide sequence encoding the immunoglobulin or analog produced by the method of claim 1.

6. Canceled

7. (Currently Amended) A cell or cell line modified to contain the DNA molecule of claim 6 5.

8. (Original) A method to produce an immunoglobulin with fully human variable region or an analog thereof which method comprises culturing the cells of claim 7 under conditions whereby said encoding nucleotide sequence is expressed to produce said immunoglobulin or analog; and recovering said immunoglobulin or analog.

9. (Original) A DNA molecule comprising a nucleotide sequence corresponding to the gene or modified gene prepared by the method of claim 3.

10. Canceled

11. (Original) A cell or cell line modified to contain the DNA molecule of claim 9.

12. (Currently Amended) A method to produce an immunoglobulin with fully human variable regions or an analog thereof which method comprises culturing the cells of claim 10 11 under conditions whereby said encoding nucleotide sequence is expressed to produce said immunoglobulin or analog; and recovering said immunoglobulin or analog.

13. (Original) A DNA molecule which comprises a nucleotide sequence encoding a variable region with desired affinity prepared according to the method of claim 4.

14. Canceled

15. (Original) A cell or cell line modified to contain the DNA molecule of claim 13.

16. (Currently Amended) A method to produce an immunoglobulin with fully human variable region or an analog thereof which method comprises culturing the cells of claim 14 15 under conditions whereby said encoding nucleotide sequence is expressed to produce said immunoglobulin or analog; and recovering said immunoglobulin or analog.

17. (Original) An immortalized B cell which secretes an immunoglobulin to a desired antigen with a fully human variable region prepared according to claim 3.

18. (Original) A method to produce an immunoglobulin or analog which comprises culturing the cells of claim 17 and recovering said immunoglobulin or analog.

19. (Original) An immunoglobulin with fully human variable region or analog produced by the method of claim 1.

20. (Original) The immunoglobulin or analog of claim 19 wherein the desired antigen is selected from the group consisting of

the leukocyte markers, CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a,b,c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27 and its ligand, CD28 and its ligands B7.1, B7.2, B7.3, CD29 and its ligand, CD30 and its ligand, CD40 and its ligand gp39, CD44, CD45 and isoforms, CDw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1 and TCR;

the histocompatibility antigens, MHC class I or II, the Lewis Y antigens, SLex, SLeY, SLea, and SLeb;

the integrins, VLA-1, VLA-2, VLA-3, VLA-4, VLA-5, VLA-6, and LFA-1;

the adhesion molecules, Mac-1 and p150,95;

the selectins, L-selectin, P-selectin, and E-selectin and their counterreceptors VCAM-1, ICAM-1, ICAM-2, and LFA-3;

the interleukins, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-11, IL-12, IL-13, IL-14, and IL-15;

interleukin receptors, IL-1R, IL-2R, IL-4R, IL-5R, IL-6R, IL-7R, IL-8R, IL-10R, IL-11R, IL-12R, IL-13R, IL-14R, and IL-15R;

chemokines, PF4, RANTES, MIP1 α , MCP1, NAP-2, Gro α , Gro β , and IL-8;

growth factors, TNFalpha, TGFbeta, TSH, VEGF/VPF, PTHrP, EGF family, FGF, PDGF family, endothelin, and gastrin releasing peptide (GRP);

growth factor receptors, TNFalphaR, RGFbetaR, TSHR, VEGFR/VPFR, FGFR, EGFR, PTHrPR, PDGFR family, EPO-R, GCSF-R and other hematopoietic receptors;

interferon receptors, IFN α R, IFN β R, and IFN γ R;

Igs and their receptors, IgE, Fc ϵ RI, and FC ϵ RII;

tumor antigens, her2-neu, mucin, CEA and endosialin;

the allergens, house dust mite antigen, lol p1 (grass) antigens, and urushiol;

the viral proteins, CMV glycoproteins B, H, and gCIII, HIV-1 envelope glycoproteins, RSV envelope glycoproteins, HSV envelope glycoproteins, EBV envelope glycoproteins, VZV envelope glycoproteins, HPV envelope glycoproteins, Hepatitis family surface antigens;

the toxins, pseudomonas endotoxin and osteopontin/uropontin, snake venom, and bee venom;

the blood factors, complement C3b, complement C5a, complement C5b-9, Rh factor, fibrinogen, fibrin, and myelin associated growth inhibitor;

the enzymes, cholesterol ester transfer protein, membrane bound matrix metalloproteases, and Glutamic acid decarboxylase (GAD); and

the miscellaneous antigens ganglioside GD3, ganglioside GM2, LMP1, LMP2, eosinophil major basic protein, eosinophil cationic protein, pANCA, Amadori protein, Type IV collagen, glycated lipids, γ -interferon, A7, P-glycoprotein and Fas (AFO-1) and oxidized-LDL.

21. (Currently Amended) A DNA molecule comprising a nucleotide sequence that encodes the immunoglobulin or analog of claim 19 ~~or 20~~.

22. Canceled

23. (Currently Amended) A cell or cell line modified to contain the DNA molecule of claim 22 21.

24. (Original) A method to produce an immunoglobulin or analog specific for the antigen selected from the group consisting of leukocyte markers, CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD11a,b,c, CD13, CD14, CD18, CD19, CD20, CD22, CD23, CD27 and its ligand, CD28 and its ligands B7.1, B7.2, B7.3, CD29 and its ligand, CD30 and its ligand, CD40 and its ligand gp39, CD44, CD45 and isoforms, CDw52 (Campath antigen), CD56, CD58, CD69, CD72, CTLA-4, LFA-1 and TCR

histocompatibility antigens, MHC class I or II, the Lewis Y antigens, SLex, SLey, SLea, and SLeb;

integrins, VLA-1, VLA-2, VLA-3, VLA-4, VLA-5, VLA-6, and LFA-1;

adhesion molecules, Mac-1 and p150,95;

selectins, L-selectin, P-selectin, and E-selectin and their counterreceptors VCAM-1, ICAM-1, ICAM-2, and LFA-3;

interleukins, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-11, IL-12, IL-13, IL-14, and IL-15;

interleukin receptors, IL-1R, IL-2R, IL-4R, IL-5R, IL-6R, IL-7R, IL-8R, IL-10R, IL-11R, IL-12R, IL-13R, IL-14R, and IL-15R;

chemokines, PF4, RANTES, MIP1 α , MCP1, NAP-2, Gro α , Gro β , and IL-8;

growth factors, TNFalpha, TGFbeta, TSH, VEGF/VPF, PTHrP, EGF family, FGF, PDGF family, endothelin, and gastrin releasing peptide (GRP);

growth factor receptors, TNFalphaR,
RGFbetaR, TSHR, VEGFR/VPFR, FGFR, EGFR, PTHrPR, PDGFR
family, EPO-R, GCSF-R and other hematopoietic receptors;

integrin receptors, IFN α R, IFN β R, and IFN γ R;

Igs and their receptors, IgE, Fc ϵ RI, and
FC ϵ RII;

tumor antigens, her2-neu, mucin, CEA and
endosialin;

allergens, house dust mite antigen, lol p1
(grass) antigens, and urushiol;

viral proteins, CMV glycoproteins B, H, and
gCIII, HIV-1 envelope glycoproteins, RSV envelope
glycoproteins, HSV envelope glycoproteins, EBV envelope
glycoproteins, VZV envelope glycoproteins, HPV envelope
glycoproteins, Hepatitis family surface antigens;

toxins, pseudomonas endotoxin and
osteopontin/uropontin, snake venom, and bee venom;

blood factors, complement C3b, complement
C5a, complement C5b-9, Rh factor, fibrinogen, fibrin, and
myelin associated growth inhibitor;

enzymes, cholesterol ester transfer protein,
membrane bound matrix metalloproteases, and glutamic acid
decarboxylase (GAD); and

miscellaneous antigens, ganglioside GD3,
ganglioside GM2, LMP1, LMP2, eosinophil major basic
protein, eosinophil cationic protein, pANCA, Amadori

protein, Type IV collagen, glycated lipids, γ -interferon, A7, P-glycoprotein and Fas (AFO-1) and oxidized-LDL

which method comprises culturing the cell or cell line of claim 23 under conditions wherein said nucleotide sequence is expressed to produce said immunoglobulin or analog; and recovering the immunoglobulin or analog.

25. Canceled

26. (Original) A antibody containing a fully human variable region or analog thereof which is specifically immunoreactive with an antigen selected from the group consisting of human IL-6, human IL-8, human TNF α , human CD4, human L-selectin, human gp39 and tetanus toxin C(TTC).

27. Canceled

28. Canceled

29. Canceled

30. Canceled

31. Canceled

32. Canceled

33. Canceled

34. (Original) The analog of claim 26 which is a single chain F_v.

35. (Original) A recombinant DNA molecule encoding the antibody or analog of claim 26.

36. (Original) A recombinant DNA molecule which comprises an expression system for the production of the antibody or analog of claim 26 which expression system comprises a nucleotide sequence encoding said antibody or analog operably linked to control sequences capable of effecting its expression.

37. (Original) A recombinant host cell which is modified to contain the DNA molecule of claim 36.

38. (Original) A method to produce an antibody or analog immunospecific for an antigen selected from the group consisting of human IL-6, human IL-8, human TNF α , human CD4, human L-selectin, human gp39 and tetanus toxin C(TTC), which method comprises culturing the cells of claim 37 under conditions wherein said coding sequence is expressed; and recovering the antibody or analog produced.

39 (Original) Use of the antibody or analog of claim 27, 29, 31 or 32 for treating an autoimmune disease in a mammal.

40. Canceled

41. Canceled

42. Canceled

43. Canceled

44. Canceled

45. Canceled